10. The composition according to claim 5, wherein said activated autologous lymphocytes is obtained by culturing autologous lymphocytes derived from a virally infected patient or an immunodeficient or immunosuppressed patient in a culture medium comprising anti-CD3 antibodies in a solid phase and interleukin-2 to proliferate, stimulate and activate said autologous lymphocytes.

11. The composition according to claim 5, wherein said activated autologous lymphocytes have no specificity or singularity.

## REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

Claims 9-11 have been added to further protect other specific embodiments of the present invention. Support for the newly added claims is readily apparent from the teachings of the specification and the original claims. Specific support can be found on page 6, lines 24-27, and page 7, line 1-2, of the specification.

With regard to the rejection of claims 5-8 under 35 USC § 102(e) as being anticipated by, or in the alternative, under 35 USC § 103(a) as being obvious over Ochoa et al. (USP 5,443,983), this rejection is deemed to be untenable and is thus respectfully traversed.

Under U.S. practice, to constitute anticipation of the claimed invention, a single prior art reference must disclose each and every material element of the claim. Further, to establish a

*prima facie* case of obviousness, the cited reference must teach or suggest the invention as a whole and include all the limitations of the claims.

The present invention is directed to activated T cells having no singularity. The activated T cells can be derived from a virally infected patient or an immunodeficient or immuno-suppressed patient. The activated T cells having no specificity according to the present invention show an excellent antiviral activity and is essentially distinct from conventional activated T cells having a singularity.

The cited Ochoa et al. reference (USP 5,443,983) teaches conventional activated T cells having a singularity which as noted above is essentially distinct from the present invention. Namely, lymphocytes applied in the medical treatment according to Ochoa et al. are not derived from a patient to be treated. Thus, it is clear from this fact that there exist a distinct difference between activated autologous lymphocytes of the present invention and that of Ochoa et al.

In further support of the differences between the lymphocytes of the present invention and that of Ochoa et al., Ochoa et al. teach that in the treatment of AIDS by administering specific T cells, the number of CD4+ T cells in the blood of the treated patient is decreasing while the amount of virus is increasing.

Other distinctions between the present invention and that of Ochoa et al. were also clearly set forth in Applicants' responses of February 12, 2001 and June 13, 2000.

Thus, for the reasons noted above, Applicants submit that the present invention is in no way anticipated or rendered obvious by the teachings and suggestion of Ochoa et al.

With regard to the rejection of claims 5-9 under 35 USC § 102(b) as being anticipated by, or in the alternative, under 35 USC § 103(a) as being obvious over Koenig, Scott et al. (Nature Med. 1 (4) 330-336 (1995)), this rejection is also deemed to be untenable for the same reasons as noted above and is thus respectfully traversed.

Koenig, Scott et al. do not teach or suggest a claimed characteristic of the present invention. Specifically, Koenig, Scott et al. do not teach or suggest *a composition comprising activated autologous lymphocytes effective against viral infections*. Like Ochoa et al., Koenig, Scott et al. disclose that, in treatment of AIDS by administering specific T cells, the number of CD4+ T cells in the blood of a treated patient is decreasing while the amount of the virus is increasing. The fact that the treatment results in decreasing CD4+ cells and increasing virus means that Koenig, Scott et al. do not teach or suggest a composition comprising activated autologous lymphocytes which is effective against viral infections and cancer.

Thus, since Koenig, Scott et al. fail to teach or suggest a key characteristic feature of the present invention, this rejection under 35 USC § 102(b) or § 103(a) cannot be sustained and should be withdrawn.

With regard to the rejection of claims 5-9 under 35 USC § 103(a) as being unpatentable over Ochoa et al. (USP 5,443,983) in view of Rosenberg, this rejection is deemed to be untenable and is thus respectfully traversed.

As stated earlier, since Ochoa et al. do not teach or suggest a composition comprising activated autologous lymphocytes effective against viral infections (for example, activated

autologous lymphocytes having no specificity or singularity), this rejection cannot be sustained and should be withdrawn.

As stated in Applicant's response of February 12, 2001, the presently claimed composition comprises "autologous" lymphocytes, which are lymphocytes that are derived from the same patient who ultimately undergoes treatment with such lymphocytes. None of the cited references including Ochoa et al. (USP 5,443,983) discloses or suggests a composition comprising activated "autologous" lymphocytes. Although the cited Ochoa et al '983 discloses an example in which peripheral blood lymphocytes (PBLs) are collected from the twin brother of a patient (see Example 4 of the reference), the twin brothers are identical in genetics, but have different activated lymphocytes.

In addition, to establish a *prima facie* case of obviousness, the cited references must provide a basis for modifying the teachings of the prior art. Further, one skilled in the art must also reasonably expect that the modification would be successful based upon the teachings and suggestions of the prior art. Here, Ochoa et al. show only a preparation of lymphocytes against tumors and does not at all teach or suggest activated autologous lymphocytes exhibiting antiviral activity. The cited reference only discusses generally the preparation of lymphocytes using anti-CD3 antibody and IL-2 which have already been reviewed in the Background section of the specification. In other words, the teachings provided by Ochoa et al. is substantially identical with JP03-80076A noted in the specification.

Likewise, the reference of Rosenberg is related to lymphocytes prepared using IL-2 only which is fundamentally distinct from the present lymphocytes using anti-CD3 in addition to IL-2.

The Rosenberg reference merely shows the generalities of IL-2 applicable for medical treatment of immune dysfunctional diseases but does not prove whether the lymphocytes prepared using only IL-2 are effective on viral infections or not. It is important to note that the cited reference Rosenberg only mentions viral infections in passing (see column 4, lines 49-54), and does not contain any data or teachings which prove and enable one skilled in the art to make and use activated autologous lymphocytes against viral infections. In fact, the reference, Nature Medicine, 1(4) pp. 330-336 (1996), discloses that lymphocytes prepared using IL-2 were not effective in remedying HIV infections, as stated on page 4 of the specification. Thus, there is clearly no teaching or suggestion in the cited references that activated autologous lymphocytes as recited in the present invention would be effective against viral infections. As a result, the teachings and suggestions of both of these references does not create a reasonable expectation of success to one skilled in the art that activated autologous lymphocytes being derived from a culture medium comprising autologous lymphocytes, anti-CD3 antibodies in a solid phase and interleukin-2 would be very effective for viral infections.

Therefore, since a *prima facie* case of obviousness cannot be established for the reason set forth above, this rejection under 35 USC § 103 cannot be sustained and should be withdrawn.

It should also be noted that the Habeshaw et al. reference (USP 5,935,579) cited by the Examiner teaches AIDS therapy using peptide vaccine with which the Applicant' invention has no connection. Although Example 2 of this reference teaches a method of activating T cells, this cited method of activating T cells ***is fundamentally the same*** as that disclosed in the references mentioned in the specification of this application, see e.g. New Eng. J. Med. 333(16),

1038(1995). Namely, this reference is related to a method for ***inducing specific T cells having antiviral activity***.

In contrast, the Applicants' invention is concerned with activated antiviral T cells having no specificity, and is, therefore, essentially distinct from the T cells of Habeshaw et al..

Although the Examiner pointed out in the last paragraph on page 3 of the Official Action, that the Applicants have not shown that their invention has a widely available antiviral spectrum, Applicants believes that the Examiner is mistaken in this regard and has not fully appreciate the significance of expermental data set forth in the specification. At present, there are antiviral preparations such as Acyclovir and Gancyclovir. These preparations are effective against a herpes simplex virus and cytomegalovirus. However, these preparations have little effectiveness against the EB virus. In light of the fact that there is no medicine currently with a curative effect on the EB virus, a person skilled in this field could understand that a medicine with a curative effect on the EB virus should be effective against the other viral infections. Accordingly, a correct evaluation of this invention cannot be made unless the Examiner correctly understand that the EB virus is extremely hard to cure.

In view of the foregoing amendments and remarks, it is respectfully submitted that the Application is now in condition for allowance. Such action is thus respectfully solicited.

If, however, the Examiner has any suggestions for expediting allowance of the application

or believes that direct communication with Applicants' attorney will advance the prosecution of this case, the Examiner is invited to contact the undersigned at the telephone number below.

Respectfully submitted,

Teruaki SEKINE et al.

By: _____

Lee Cheng
Registration No. 40,949
Attorney for ApplicantS

LC/gtn
Washington, D.C. 20006-1021
Telephone (202) 721-8200
Facsimile (202) 721-8250
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